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Remote Photoregulated Ring Gliding in a [2]Rotaxane via a Molecular Effector

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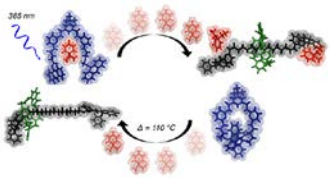
Supporting Information Placeholder



ABSTRACT: A molecular barbiturate messenger, which is reversibly released / captured by a photoswitchable artificial molecular receptor, is shown to act as an effector to control ring gliding on a distant hydrogen-bonding [2]rotaxane. Thus light-driven chemical communication governing the operation of a remote molecular machine is demonstrated using an information-rich neutral molecule.

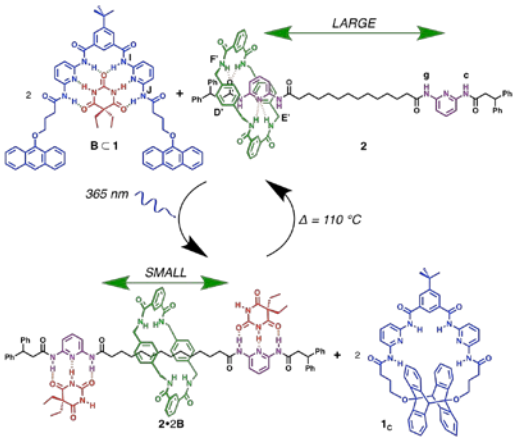
Chemical communication is ubiquitous in nature and is notably moderated by ion transfer in neurons, muscle contraction and mammalian vision.[1] Equally, molecules such as hormones constitute a major signaling pathway in the endocrine system.[2] On the other hand, while a wealth of photoionic systems is known,[3] artificial molecular systems[4] utilizing chemical transfer between functional molecules are scarce and typically rely on transfer of metal ions or protons.[5] Concerning the latter, photoactive variants have been reported using spiropyran chromophores for reversible ion binding.[6] Utilization of molecules, rather than ions, as messengers in such a scheme has not been duly considered. Molecules offer the advantage of greater structural diversity and are inherently information-rich. Here we report a unique supramolecular system, where photomodulation of the amplitude of the translational motion of a macrocycle along the thread of a two-station [2]rotaxane is achieved by the intermediacy of a molecular effector, which is reversibly taken-up / released by a distinct switchable receptor.

In order to design such a system, a judicious combination of functional molecules is required. The receptor should be a bistable species where one form binds the molecular effector strongly ($K_{ass}1$), while conversely in the second state, binding is much weaker ($K_{ass}1'$), such that $K_{ass}1 >> K_{ass}1'$. Ideally interconversion should be triggered by an external stimulus without chemical build up. Molecule **1** (Scheme 1) strongly binds barbital (**B**) in its open form ($K_{ass}1$ = 38,000 M^{-1}) using 6 hydrogen-bonds (with H-bonding pattern DADDAD:ADAADA).[7] Photoirradiation of **1** effects a [4π+4π] anthracene cyclomerisation reaction giving $\mathbf{1_C}$, rendering the receptor site ill-adapted to accommodate **B** ($K_{ass}1'$ ≤ 10 M^{-1}), thereby promoting photorelease and transfer of autonomous effector **B**.

In order to demonstrate photopromoted transfer of **B**, a second hydrogen-bonding molecule is required with an affinity for **B** ($K_{ass}2$) that is intermediate between **1** and $\mathbf{1_C}$, i.e. $K_{ass}1 > K_{ass}2 > K_{ass}1'$. Benzylic amide rotaxane **2** having two diamidopyridine units can bind **B** to form 1:1 and 1:2 complexes with stability constants $K_{ass}2$(1:1) = 787 M^{-1}; $K_{ass}2$(1:2) 108 M^{-1}, respectively.[8a,b] Indeed, this ordering may be anticipated based on the number of available hydrogen bonds formed between a barbital guest and **1**, **2** and $\mathbf{1_C}$, namely 6 (with H-bonding pattern DADDAD:ADAADA) vs 3 (DAD:ADA) vs <3, respectively. Additionally, considering translational motion of the ring in **2**, some of us reported that guest binding at both rotaxane diamidopyridine sites had a direct influence on the amplitude of the ring shuttling.[8,9] Therefore, as represented in Scheme 1, in the initial state **B** would be anticipated to reside quasi-exclusively at receptor **1** and an unimpeded, large amplitude translational motion of the macrocycle would occur in rotaxane **2**. Photoirradiation would provoke release of **B**, chemical transfer and effective

chemical communication with the rotaxane, thereby restricting the forward and backward ring motion through the formation of a ternary aggregate (**2B•2**).

Scheme 1 A supramolecular system where photoregulated binding of a barbiturate messenger modulates the amplitude of the translational motion of a ring in an interlocked architecture.



Hydrogen-bonding between amide functions of **1** / **2** and imide functions of messenger barbiturate **B** was followed by ^{1}H NMR and UV-vis spectroscopies. Thus the state of the system and average instantaneous position of effector and ring components could be read-out. Based on relative and absolute association constants for **B** with receptor **1** and rotaxane **2**, a mixture of **1**, **B** and **2** ensuring preponderant complexation at **1** (89 % **B⊂1**; ≈ 2 % **2B•2**) was determined to be a molar ratio of 1:1:0.5, respectively at 2 mM concentration of **1**.[7,8] Following irradiation, a dramatic population inversion was anticipated (**B⊂1$_C$** ≈ 2 %; **2B•2** = 65 %). Direct titration of barbiturate into mixtures of **1** and **2**, or **1$_C$** and **2** gave similar values, showing the rapid redistribution of **B** (Figure S1 and S2) compatible with reversible binding. Furthermore, moderate barbiturate binding-induced fluorescence quenching of **1** was observed (from Φ_f = 0.32 to Φ_f = 0.27 for **B⊂1** (20:1, [**1**] = 5 μM), Figure S6).[7,10] Meanwhile, addition of [2]rotaxane **2** to **1** did not perturb the emission (Φ_f = 0.31; 1:0.5, [**1**] = 5 μM).[7]

^{1}H NMR spectra in Figure 1 show the various states of the system,[11] denoted by the chemical shifts of H-bonding N-H resonances of **1** and **B**. The spectrum of the **B⊂1+2** mixture (1:1:0.5; [**B**] = 2 mM, Figure 1b) shows a marked difference between the amide protons H_c and H_g of **2**, imide protons H_I and H_J of **B** compared to the mixture in presence of cyclized **1$_C$** (**2B•2+1$_C$**; 1:1:0.5, [**B**] = 2 mM, Figure 1e). Addition of **B** (1 equiv.) to the acyclic receptor **1** (2 mM, CD_2Cl_2, Figure 1a and S3b) resulted in strong downfield shifts of the N-H resonances of **B** ($\Delta\delta$ = 3.70 ppm) and those of the amide protons of the receptor ($\Delta\delta$ = 1.25 and 1.30 ppm), *c.f.* Figures S3a and S3c. Meanwhile, in the case of poorly binding **1$_C$** (2 mM, CD_2Cl_2, Figures 1f and S3d), addition of **B** resulted in small downfield shifts of the corresponding barbiturate ($\Delta\delta$ = 0.50 ppm) and receptor ($\Delta\delta$ = 0.15 and 0.05 ppm) resonances. Addition of **B** (2 equiv.) to the homoditopic [2]rotaxane **2** (1 mM, CD_2Cl_2, Figure 1d and S4) results in formation of **2B•2**, as indicated by downfield shifts of imide NH protons of barbiturate messenger ($\Delta\delta$ = 0.50 ppm) as well as NH amide protons (H_c and H_g) of [2]rotaxane ($\Delta\delta$ = 0.30 ppm and 0.29 ppm) compared to uncomplexed **B** (Figure S4c) and **2** (Figure 1c and S4a). This complexation with the **2** induces a restriction of the translational motion amplitude of the macrocycle of the interlocked architecture shown by small downfield proton resonance shifts compared to the free [2]rotaxane (Figure S4).[8a] Further evidence for the feasibility of the transfer system came from the non interaction between receptor **1** and [2]rotaxane **2** (Figure S5). The ensemble of these observations is consistent with an effective transfer of guest **B** between acyclic receptor **1** and the target rotaxane **2**.

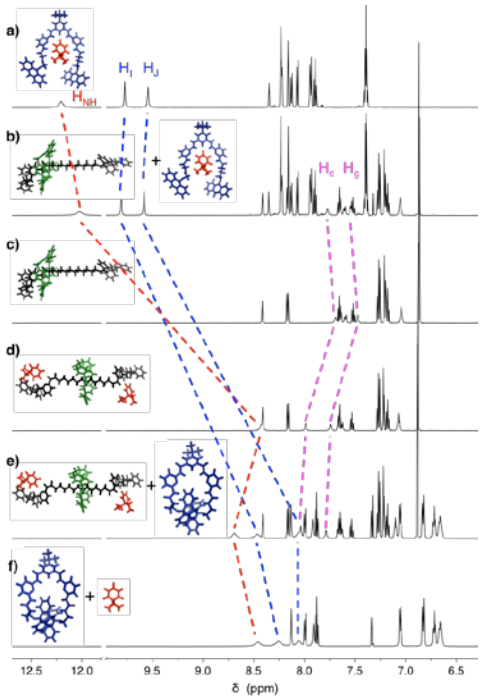


Figure 1. Partial ^{1}H NMR spectra (600 MHz, CD_2Cl_2, 298 K) of: a) a mixture of **1** and **B** (1:1, [**B**] = 2 mM); b) a mixture of **1**, **B** and **2** (1:1:0.5, [**B**] = 2 mM); c) **2** (1 mM), d) complex **2B•2** (1:0.5, 2 mM); e) mixture ofs **1$_C$**, **B** and **2** (1:1:0.5, 2 mM); f) mixture of **1$_C$** and **B** (1:1, [**B**] = 2 mM). Assigned resonances correspond to labelled protons in Scheme 1 (see the Supporting Information, SI, for full attribution). Space-filling structures generated by PM6 modeling.

Photoinduced evolution of **B⊂1+2** (1:1:0.5, CD_2Cl_2, [**B**] = 2 mM) was followed by ^{1}H NMR spectroscopy (Figure 2 and S7) as a function of irradiation time (λ = 350-

400 nm, see SI for irradiation conditions. Degassed solutions were used throughout this study). A gradual upfield shift of the imide NH protons of **B** ($\Delta\delta$ =12.1 to 8.6 ppm) and disappearance of NH amide protons of receptor **1** were synchronous with the appearance of **1**$_C$. Complete disappearance of anthracene proton signals (δ = 7.90-7.95 and 7.48-7.42 ppm in CD_2Cl_2) of the acyclic receptor **1** (Figure 2) was observed and four multiplet signals assigned to the aromatic protons of the dimerized anthracene moiety in receptor **1**$_C$ appeared at 6.65, 6.72, 6.85 and 7.09 ppm, after cyclisation of receptor **1**. A downfield shift of the H_c and H_g NH proton signals was observed relative to the mixture **2B•2** (Figure S4b), associated with a restriction of ring shuttling amplitude induced by the complexation of **B** on the ditopic [2]rotaxane **2**. Thermal reversibility was studied by heating to 110 °C, resulting in retrocyclomerisation of **1**$_C$, as judged by ^{1}H NMR (Figure S8). After 780 min, quasi-complete return of the system to its initial state was noted.

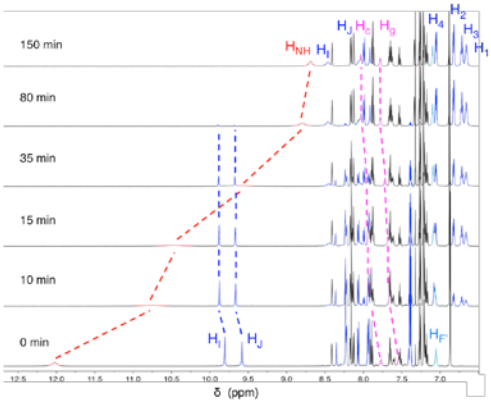


Figure 2. ^{1}H NMR spectra (300 MHz, CD_2Cl_2, 298 K) of a mixture of **1**, **B** and **2** (1:1:0.5, [**B**] = 2 mM) after irradiation (λ = 350-400 nm) for 0, 10, 15, 35, 80 and 150 min.

Dynamic ordering spectroscopy (DOSY) NMR experiments gave further information on the formation of supramolecular aggregates of increased mass/hydrodynamic radius. This translates into a lowered diffusion rate for both constituent components, allowing instantaneous determination of the messenger position.[12] Free **B**, being a small, highly mobile molecule (average diffusion coefficient (D) of 14.6×10^{-10} m^{2}s^{-1} in CD_2Cl_2, Figure S13) was used as a probe to follow its complexation. In the presence of receptor **1** its diffusion rate slows (13.0×10^{-10} m^{2}s^{-1}, Figure S11a) showing association in solution, while photoirradiation and subsequent molecule release, increases its diffusion rate value (14.4×10^{-10} m^{2}s^{-1}, Figure S11b), showing lower association with **1**$_C$. Upon irradiation of the system **B**⊂**1**+**2** (1:1:0.5, [**B**] = 2 mM) for 3 h, the measured weighted average diffusion coefficient of the barbiturate messenger increased from 9.8×10^{-10} m^{2}s^{-1} to 12.9×10^{-10} m^{2}s^{-1} (Figure 3a and b). The lowering of the diffusion coefficient D of the rotaxane (from 5.6×10^{-10} m^{2}s^{-1} to 5.3×10^{-10} m^{2}s^{-1}) and the D increase of the barbiturate upon photoirradiation of the three component mixture is indicative of the photo-transfer process. Analysis of ^{1}H spectra acquired over a wide range of temperatures is commonly used to obtain information on fast molecular dynamic processes, such as the ring movement rate. Thus by observing the coalescence of resonances at low temperature (see SI for description and Figs. S14-S15), the rate of exchange/ring shuttling between identical stations in **2** could be estimated at 4900 s^{-1} at 223 K. Meanwhile, the presence of **B**, in otherwise analogous conditions, a higher exchange value (14000 s^{-1}) was measured. This infers that the photoregulated remote effector can modulate not only the magnitude but also the nett velocity of the ring movement within the rotaxane.

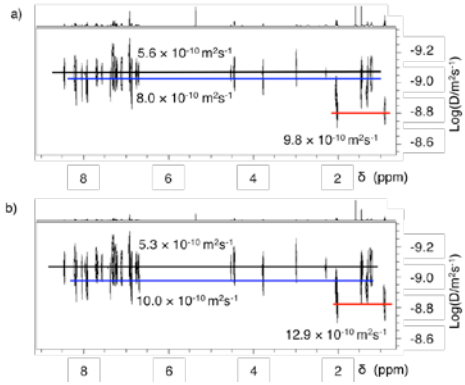


Figure 3. DOSY NMR spectra (600 MHz, CD_2Cl_2, 298 K) of a mixture of **1**, **B** and **2** (1:1:0.5, [**B**] = 2 mM): (a) before irradiation; (b) after irradiation (λ = 350-400 nm) for 150 min.

Photomodulation of the mixture of receptor **1**, [2]rotaxane **2** and barbital (1:0.5:1, [**B**] = 2mM) in dichloromethane was further followed by UV-vis and fluorescence spectroscopy. The structured absorption band (330-400 nm) of **1** disappeared upon photodimerisation (λ = 365 nm in degassed CH_2Cl_2), yielding non-binding **1**$_C$ (Figure 4). This allowed studies of the evolution of the release of barbital as a function of the irradiation time. Quantum yield determination (Φ_r)[13] of the photodimerisation reactions afforded a measure of the efficiency of the photoprocesses for the system (receptor **1** in presence and in absence of barbital and [2]rotaxane **2**). These yields were invariant at micro-to-millimolar concentrations, consistent with an intramolecular reaction, while the presence of rotaxane did not affect the determined value.[7]

Reversible disassembly of the photoadduct (Scheme 1) allows system reset, and subsequent stimulus-triggered cycles. Reversibility of the photocontrol process over multiple cycles was studied using a mixture of **1**, **B** and **2** (Figure 4c), by repeated cycles of: irradiation at 365 nm for 3 h, and thermal retrodimerisation at 110 °C over 14 h. The percentage of **1**$_C$ after each opening process was determined by absorption changes at 370 nm. A fatigue study showed that >94 % of the anthracene chromophore was

recovered after each cycle (Figure 4c), with a total fatigue of 16 % after 4 cycles. Photochemical reversion on irradiating the (λ = 280 nm) resulted in a higher degree of fatigue and build-up of irreversible photoproducts.[14]

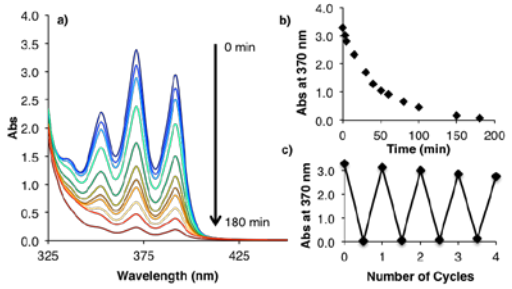


Figure 4. a) Electronic absorption spectra (1 mm pathlength) of a mixture of **1**, **B** and **2** (1:1:0.5, [**B**] = 2 mM) in CH_2Cl_2. On irradiation (λ = 350-400 nm) the disappearance of the anthracene moieties ($Abs_{370\ nm}$, see Fig. 4b) continued to 94 % conversion; c) Cycles of photoirradiation and thermal reversion, corresponding to shuttling of **B** between **1** and **2**.

In conclusion, combination of a photoswitchable receptor for a neutral multiple hydrogen-bonding molecular effector and a two-station [2]rotaxane constitutes a system where modulation of the ring shuttling is controlled remotely, via the intermediacy of a neutral molecule. This system was implemented based on knowledge of binding constants and absorption profiles and opens the way to future phototriggered supramolecular systems involving chemical communication with a diversity of molecular species. Ongoing work concerns development of biocompatible systems to interface biomacromolecules.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, fluorescence spectra, ^{1}H NMR characterization data and diffusion ordered NMR of **1**, **2**, $\mathbf{1_C}$, **B** and different mixture **B⊂1**, **B⊂$\mathbf{1_C}$**, **2B•2**, **B⊂1+2**, **2B•2+$\mathbf{1_C}$**, **2+1** and **2+$\mathbf{1_C}$**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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